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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup> :</b> <b>C07F 9/38</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 96/19485</b> <b>(43) International Publication Date:</b> 27 June 1996 (27.06.96)
<b>(21) International Application Number:</b> PCT/SI95/00029 <b>(22) International Filing Date:</b> 18 December 1995 (18.12.95) <b>(30) Priority Data:</b> P-9400449 20 December 1994 (20.12.94) SI <b>(71) Applicant (for all designated States except US):</b> PINUS D.D. [SI/SI]; Grajski trg 21, 62327 Rače (SI). <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only):</b> BAUMAN, Davorin [SI/SI]; Mariborska c. 81, 62327 Rače (SI). KNEZ, Željko [SI/SI]; Wilsonova 15, 62000 Maribor (SI). MARČINKO, Vlasta [SI/SI]; Račka c.16, Hotinja vas, 62312 Orehova vas (SI). PETROVIČ, Branko [SI/SI]; Kardeljeva 73, 62000 Maribor (SI). RIŽNER, Andreja [SI/SI]; C. talcev 13, 62327 Rače (SI). <b>(74) Agent:</b> AVRELIJA GRAD-GORIUP, D.O.O.; Celovška 93a, 61000 Ljubljana (SI).		<b>(81) Designated States:</b> AU, BG, BR, BY, CA, CN, CZ, EE, FI, HU, IS, JP, KR, LT, LV, MK, MX, NO, PL, RO, RU, SK, UA, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
<b>(54) Title:</b> PROCESS FOR PREPARING N-PHOSPHONOMETHYL GLYCINE  <b>(57) Abstract</b>  Process for preparing N-phosphonomethyl glycine by wet oxidation of N-(phosphonomethyl)iminodiacetic acid with an oxygen enriched air or with hydrogen peroxide at pressures of 100 - 1000 bar, at temperatures of 50 - 500 °C, and reaction times of 0.01 - 10 hours. The process may be performed at subcritical, or preferably supercritical conditions of wet oxidation of N-(phosphonomethyl)iminodiacetic acid. The process is preferably continuous. N-phosphonomethyl glycine, known under the generic name glyphosate, in an active substance indicated for the use in ecologically appropriate herbicides.		

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## 5                   PROCESS FOR PREPARING N-PHOSPHONOMETHYL GLYCINE

10       The present invention relates to a new process for the preparation of N-phosphonomethyl glycine.

15       N-phosphonomethyl glycine, known under the generic name **glyphosate** as it will be used in the following text of the description, claims, and abstract for the characterisation of N-phosphonomethyl glycine, is an active substance used in ecologically appropriate herbicides. Such herbicides act on numerous annual or perennial, grass or broad-leaved, woody or other weeds. They are used for the control of weeds in stubble fields, in vineyards, orchards, canals, swamps, grasslands, pasture-lands, drained areas, woods, non-cultivated areas, railway tracks, dams and in other places.

20       Glyphosate acts on the system and is rapidly transferred into all vital plant organs (roots, rhizome); therefore plants are completely destroyed by herbicides containing it.

25       From the discovery (US Patent No. 3,950,402) of the outstanding herbicidal activity of glyphosate there were synthesised several derivatives, homologues and analogues thereof. However, glyphosate and its water soluble salts still exhibit the major herbicidal activity.

30       Glyphosate encompasses many excellent biological properties: a broad activity spectrum, a non-selective and efficient activity on a high number of annual and perennial weeds. One of its most important properties is the rapid transfer from the plant's leaves into its roots, and thus radically destroying the weeds.

35       The herbicide glyphosate is rapidly adsorbed by the soil where its herbicidal activity is very much diminished. A slight quantity of glyphosate is decomposed *via* chemical reactions, the majority, however, is decomposed by means of micro-organisms into nutrients for plants, such as: phosphoric acid, ammonia and carbon dioxide.

The potential metabolic pathway is described in US Patent No. 3,950,402. Details on the glyphosate metabolism in plants are not well-known.

The current knowledge about the characteristics of glyphosate does not indicate that this herbicide would cause after the application unexpected damage to the soil and the environment. The herbicide itself is also non-polluting for the environment and is practically non-toxic for mammals, birds, fish, insects, and *bacteriae*.

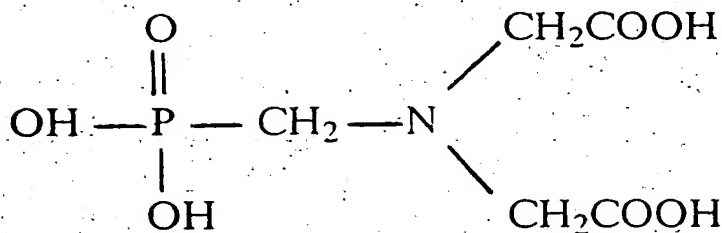
Toxicity of glyphosate:

- acute oral LD<sub>50</sub> for rats: 5600 mg/kg,
- acute oral LD<sub>50</sub> for rabbits: 3800 mg/kg,

N-phosphonomethyl glycine, generic glyphosate, is a secondary amine of the empirical formula C<sub>3</sub>H<sub>8</sub>NO<sub>5</sub>P and the chemical formula

15

20



Glyphosate is a white crystalline solid substance. The solubility of glyphosate in water is low, as evident from the following Table 1.

25

Temperature (°C)	Solubility (%)
10	1.60
25	4.19
35	5.95
45	7.70
55	9.56

Glyphosate is also practically insoluble in the majority of organic solvents, which is an indication for very strong intermolecular hydrogen bonds in its crystalline structure. It is soluble in acids, bases and amines.

30

Hitherto, several processes for preparing glyphosate have been known.

1. US Patent 3,950,402.

There is described the preparation of glyphosate by means of oxidation of N-(phosphonomethyl)iminodiacetic acid with an oxidising agent, such as hydrogen peroxide or a gas containing free oxygen. In the case of using hydrogen peroxide as an oxidising agent, initially the mixture of N-(phosphonomethyl)iminodiacetic acid, water and conc.  $H_2SO_4$  is heated and then under stirring 30%  $H_2O_2$  is added. The stirring is continued till the formation of a colourless solution. The cooling starts the precipitation of glyphosate which is isolated by filtration. When applying a gas containing free oxygen as an oxidising agent the pressure vessel or a glass reaction vessel are filled with a mixture of N-(phosphonomethyl)iminodiacetic acid, water and 5% palladium, rhodium, platinum or iridium on carbon.

The mixture is heated to 70 - 120 °C and oxygen or pressurised air are continuously fed in. The mixture is then cooled down to room temperature. The catalyst is separated by filtration, and the filtrate sucked off.

2. YU Patent application No. P-1175/75 Monsanto Company.

In this process a pressure vessel is filled with a mixture of N-(phosphonomethyl)iminodiacetic acid, water and active carbon. Then pressurised air is fed in. It is important, that the specific surface of the active carbon is sufficient (400 - 1600 m<sup>2</sup>/g). The reaction temperature is 90 - 150 °C. The pressure range is 0.5 - 203 bar. The most preferred pressures are 1 - 7 bar.

3. YU Patent 35,771 Monsanto Company.

In this process N-(phosphonomethyl)iminodiacetic acid is mixed at increased temperature with a strong acid having a  $pK_a$  under 2.2. This results in the hydrolysis of N-(phosphonomethyl)iminodiacetic acid into glyphosate and other products. The reaction mixture is then diluted with water and an organic water miscible solvent. Glyphosate precipitates.

4. US patent 5,043,475.

Described is a process for preparing glyphosate by means of oxidation with N-(phosphonomethyl)iminodiacetic acid with peroxide, yielding the intermediate N-(phosphonomethyl)iminodiacetic acid N-oxide. N-(phosphonomethyl)iminodiacetic acid, water and hydrogen peroxide are heated to 20 - 65 °C in the presence of a catalyst, such as a water soluble molybdenum or wolfram (tungsten) salt. After some

time the solution is cooled down and then a water soluble salt of vanadium, iron or copper. The temperature should not exceed 65 °C. Glyphosate precipitates and is isolated by filtration.

5. YU Patent 37,363 Monsanto Company.

According to this process N-organo-N-(phosphonomethyl)aminodiacetic acid is dissolved in v HCl. In an electrolytic cell (graphite anode, platinum cathode or a graphite cathode) proceeds the oxidation into N-phosphonomethyl glycine. The reaction may be performed at a temperature of 0 - 110 °C. The reaction time is dependant on the current density, concentration on the electrode surface and the volume of the reaction solution. The glyphosate may be isolated by means of extraction and recrystallisation, centrifugation, concentration and the like.

6. US Patent 4,684,483.

Described is a process for the synthesis of N-substituted amino acids. To glyoxal in aqueous medium is added SO<sub>2</sub>, resulting in the formation of a sulphonated intermediate. Then the nitrogen component (primary or secondary amine, ammonia) is added. The reaction temperature is 80 - 90 °C.

7. WO 90/06929, Monsanto Company.

N-Benzyl-N-phosphonomethyl glycine and its esters in debenzylation with hydrogen halide acids yield benzyl halides and glyphosate or its esters. The reaction temperature is 40 - 100 °C.

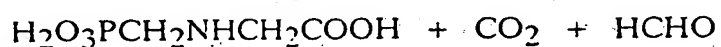
8. US Patent 3,927,080.

The process relates to the preparation of glyphosate by means of acid (HCl, HBr, HI) catalysed hydrolysis of N-t-butyl-N-phosphonomethyl glycine and its esters. The reaction temperature is 110 - 130 °C.

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There has now been found a new process, which is the object of the present invention, yielding N-phosphonomethyl glycine denominated glyphosate. Contrary to prior art processes this process proceeds without the use of catalysts in conformance with the following Reaction Scheme.

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In accordance with the present invention glyphosate is obtained by means of wet oxidation of N-(phosphonomethyl)iminodiacetic acid. As oxidising agent air enriched with oxygen or hydrogen peroxide are used at pressures of 100 - 1000 bar. The reaction temperature is 50 - 500 °C, the duration of the reaction is 0.01 - 10 hours. The wet oxidation proceeds in accordance with the present invention, in the following way:

A) At subcritical conditions ( $T < 374\text{ }^{\circ}\text{C}$ ) and

B) At supercritical conditions ( $T > 374\text{ }^{\circ}\text{C}$ ,  $P > 220\text{ bar}$ ).

10 A) The wet oxidation at subcritical conditions. It is performed in aqueous phase at temperatures of 150 - 300 °C and pressures 100 - 150 bar. This embodiment of the invention is bound by several restrictions. Upon mixing air and an aqueous solution of the substance the oxygen solubility in water is significantly lower than the solubility required for the complete oxidation. A two-phase mixture is in the reactor. Since the  
15 oxidation is not complete, the gas leaving the process contains significant concentrations of the volatile organic components and has to be usually purified prior to the release into the atmosphere.

B) Supercritical wet oxidation in accordance with the present invention is an  
20 embodiment upgrading the wet oxidation. The efficiency is much improved, and the investment costs are significantly diminished.

The process comprises a wet oxidation of organic components in an aqueous phase at conditions over the water critical point ( $T_c = 374\text{ }^{\circ}\text{C}$ ,  $P_c = 220\text{ bar}$ ). The basic  
25 characteristic is the existence of oxygen, water and organic substances at supercritical conditions in a single homogeneous fluid phase. In the procedure a 30% hydrogen peroxide solution and a 1-50%, preferably 1-40%, especially 9-10% aqueous solution of N-(phosphonomethyl)iminodiacetic acid.

30 The supercritical water is an excellent medium in which organic substances are oxidised as a result of high solubility of organic components and oxygen. The relatively high temperature guarantees a rapid oxidation. The process must be performed in a corrosion resistant reactor.

35 The most important advantages of the performance of the process in accordance of the present invention at supercritical conditions are:

- the increased solubility of oxygen in water; thus resulting in a single phase;

- the rapid oxidation of organic substances which enables the adiabatic conditions and a high initial temperature and a short reaction time;
- a complete oxidation of the organic substances; for this reason the purification of the exhaust gases is not needed;
- 5    - the separation of precipitated inorganic components;
- the heat generated in the decomposition of the substances is used in the heating of the supercritical water.

The reaction conditions are dependant from:

- 10    - the phase balance of the system water : organic substance,
- the phase balance of the system water : oxygen,
- the ignition temperature of the system water : organic substance : oxygen, which is dependant on the pressure and composition of the mixture.

- 15    The process in accordance with the present invention may be performed in one of the apparatus schematically represented on Fig. 1 and Fig. 2.

On Fig. 1 is represented an apparatus for the charge performance of the process in accordance with the invention.

20

On Fig. 2 is represented an apparatus for the continuous performance of the process in accordance with the invention.

The reference numerals stand for:

- 25    1 - high-pressure pump
- 2 - valve
- 3 - one-way valve
- 4 - safety valve
- 5 - needle valve
- 30    Pi - manometer.

The process in accordance with the present invention is illustrated by the following Examples, however, without limiting its scope.



Example 1

Into the reactor represented on Fig. 1 were charged 170 mls of water and 15 g of N-(phosphono-methyl)iminodiacetic acid. The reaction mixture was heated to 250 °C, and after that air enriched with oxygen (50%) was blown into it. The pressure in the reactor was 200 bar. In the cell a constant pressure was kept up, and the air flow was 0.1 - 10 g/min. The temperature was maintained by means of a heating jacket. The duration of the reaction was 10 minutes.

Glyphosate was isolated by concentrating the filtrate under reduced pressure in a rotary evaporator, or left to cool down and then sucked off. The formed crystals were dried in a drier for 2 hours at 105 °C. The crystals were analysed by HPLC. The synthesis yield was 80%.

Example 2

Into the reactor represented on Fig. 1 were charged 170 mls of water and 15 g of N-(phosphono-methyl)iminodiacetic acid. The reaction mixture was heated to 250 °C, and after that air enriched with oxygen (50%) was blown into it. The pressure in the reactor was 500 bar. In the cell a constant pressure was kept up, and the air flow was 0.1 - 10 g/min. The temperature was maintained by means of a heating jacket. The duration of the reaction was 10 minutes.

Glyphosate was isolated by concentrating the filtrate under reduced pressure in a rotary evaporator, or left to cool down and then sucked off. The formed crystals were dried in a drier for 2 hours at 105 °C. The crystals were analysed by HPLC. The synthesis yield was 92%.

Example 3

Into the reactor represented on Fig. 1 were charged 170 mls of water and 15 g of N-(phosphono-methyl)iminodiacetic acid. The reaction mixture was heated to 400 °C, and after that air enriched with oxygen (50%) was blown into it. The pressure in the reactor was 500 bar. In the cell a constant pressure was kept up, and the air flow was 0.1 - 10 g/min. The temperature was maintained by means of a heating jacket. The duration of the reaction was 5 minutes.

Glyphosate was isolated by concentrating the filtrate under reduced pressure in a rotary evaporator, or left to cool down and then sucked off. The formed crystals were dried in a drier for 2 hours at 105 °C. The crystals were analysed by HPLC. The synthesis yield was 94%.

5

#### Example 4

Into the cell were charged 50 mls of water and 15 g of N-(phosphonomethyl)-iminodiacetic acid, whereupon the desired pressure was generated by means of water. Then 20 mls of hydrogen peroxide (30%) were added. The reaction mixture was heated to 400 °C, and after that air enriched with oxygen (50%) was blown into it. The pressure in the reactor was 500 bar. In the cell a constant pressure was kept up, and the air flow was 0.1 - 10 g/min. The temperature was maintained by means of a heating jacket. The duration of the reaction was 5 minutes.

15

Glyphosate was isolated by concentrating the filtrate under reduced pressure in a rotary evaporator, or left to cool down and then sucked off. The formed crystals were dried in a drier for 2 hours at 105 °C. The HPLC analysis showed that the crystals contained practically pure N-(phosphonomethyl)glycine. The synthesis yield was 93%.

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#### Example 5

Into a continuous reactor shown on Fig. 2 functioning under a pressure of 200 bar and at a temperature of 250 °C, was continuously pumped the solution of 9-10% N-(phosphonomethyl)iminodiacetic acid in water. By means of the pump B a 30% solution of hydrogen peroxide was charged into the system.

25

The duration of the reaction was varied in the range of 1 - 100 minutes.

30

In the reaction product the glyphosate content was analysed. The reactor conversion range grade was 92%.

#### Example 6

35

Into a continuous reactor shown on Fig. 2 functioning under a pressure of 400 bar and at a temperature of 400 °C, was continuously pumped the solution of 9-10% N-(phosphonomethyl)iminodiacetic acid in water. By means of the pump B a 30%

solution of hydrogen peroxide was charged into the system. The duration of the reaction was varied in the range of 1 - 100 minutes.

In the reaction product the glyphosate content was analysed. The reactor conversion  
5 range grade was 94%.

## CLAIMS

- 5 1. A process for preparing N-phosphonomethyl glycine by oxidation of N-(phosphonomethyl)iminodiacetic acid, characterised by the performance of a wet oxidation of N-(phosphonomethyl)iminodiacetic acid with hydrogen peroxide or with an oxygen enriched air at pressures of 100 - 1000 bar, at temperatures of 50 - 500 °C, and reaction times of 0.01 - 10 hours.
- 10 2. A process as claimed in claim 1, characterised in that it is performed at wet oxidation subcritical conditions.
- 15 3. A process as claimed in claim 1, characterised in that it is performed at wet oxidation supercritical conditions.
4. A process as claimed in claim 1 and 3, characterised in that it is performed in a continuous way.

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PINUS d.d.

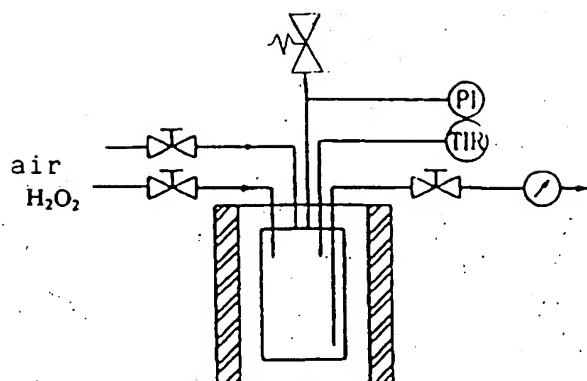


Fig. 1

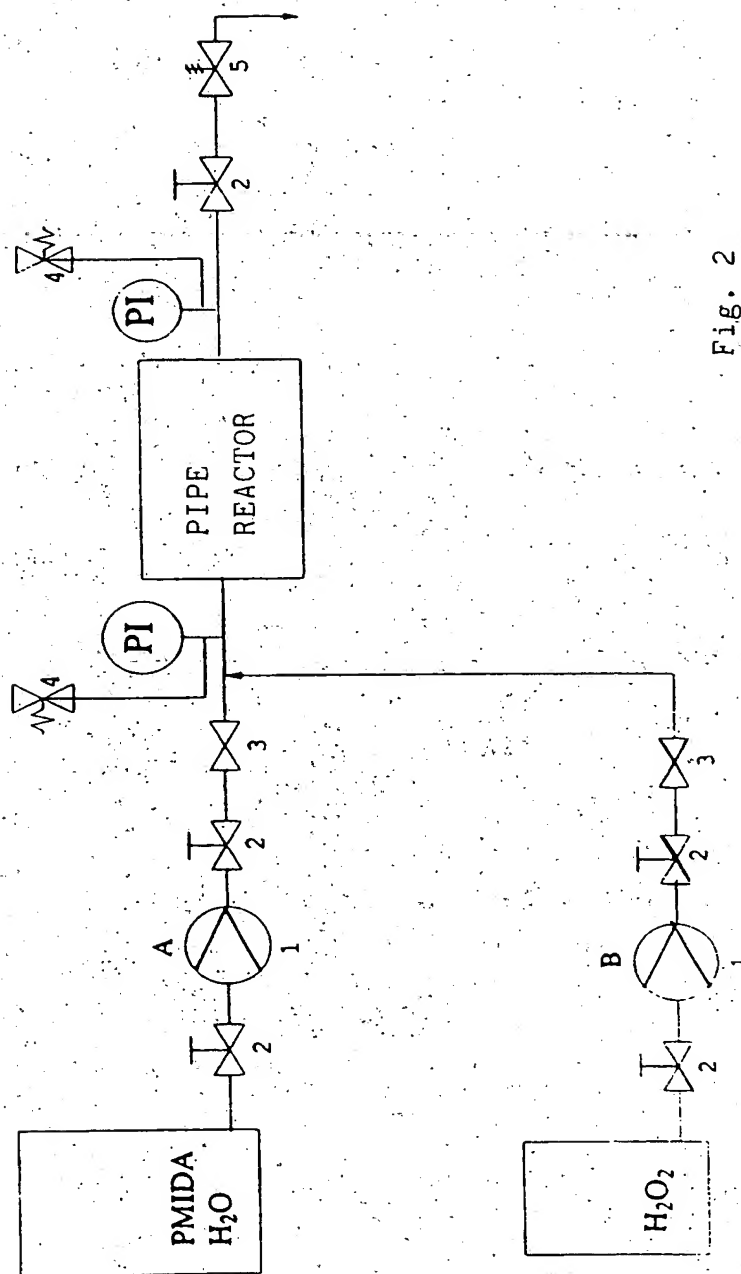


Fig. 2

## INTERNATIONAL SEARCH REPORT

International Application No.

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07F9/38

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FR,A,2 186 477 (MONSANTO CO.) 11 January 1974 see the whole document	1-4
Y	EP,A,0 019 445 (NITROKEMIA IPARTELEPEK) 26 November 1980 see the whole document	1-4
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Date of the actual completion of the international search

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Date of mailing of the international search report

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